Outcome in Patients with Acute Limb Ischemia Post Hybrid Procedure Compared to Surgical Thrombectomy

Purnama Satria Bakti^{a*}, Nyityasmono Tri Nugroho^{a,b}, Dedy Pratama^a

Introduction: Acute limb ischemia (ALI) is characterized by decreased perfusion to extremities in the form of acute ischemia and the presence of acute thrombus which may endanger the viability of the extremities. Therapeutic modalities are various including intraarterial thrombolysis with or without the help of ultrasonography and the use of thrombectomy instruments. However, due to the high morbidity and mortality rate, a new technique called the hybrid procedure is introduced. This procedure is a combination between endovascular management to correct the abnormalities with the help of angiography as well as thrombectomy surgical management, in the same time. Therefore, it is necessary to conduct a literature search related to the case we are reporting, to determine whether hybrid procedure or thrombectomy only is the best management for ALI. This study aims to determine the best management for the case being reported according to literature search and critical reviews collected from medical research database.

Method: From the data collected, there was one interesting case, which is a case about acute limb ischemia, and the following operative management. Afterwards, a literature search was conducted to obtain articles related to the case, and critical review was made regarding the selected article.

Results: At the end of the literature search, we found two articles which showed better outcome on hybrid procedure compared to surgical thrombectomy. Compared to the group who underwent thrombectomy, there was decreased 30-days mortality in the group who underwent the hybrid procedure (3.3% vs 4.4%, *p*-value 0.05), decreased incidence of amputations after 30 days (6.49% vs 13.5%, *p*-value 0.023), increased limb salvage (91.9% vs 82.3%, *p*-value 0.03, 95% CI), and decreased two-years mortality (18.7% vs 40.5%; *p*-value <0.001).

Conclusion: Critical review on articles obtained from literature search in online database showed that the outcome hybrid procedure was better than surgical thrombectomy only.

Keywords: acute limb ischemia; hybrid procedure; thrombectomy; outcome
<https://doi.org/10.36864/jinasvs.2020.2.013>

Copyright © 2020, The Indonesian Society for Vascular and Endovascular Surgery

JINASVS 2020;1(2):55-60

*Correspondence: satriasurgery@gmail.com

^aM.D., Vascular and Endovascular Division, Department of Surgery, Cipto Mangunkusumo Hospital - Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

^bM.D., Department of Vascular and Endovascular Surgery, University Hospital of Muenster, Muenster, Germany

INTRODUCTION

Acute limb ischemia (ALI) is characterized by decreased perfusion to extremities in the form of acute ischemia (<14 days), and the presence of acute thrombus which may endanger the viability of the extremities^{1, 2}. Various endovascular procedures are available to manage subjects with ALI in order to return arterial blood flow and to treat any existing thrombus. Available therapeutic modalities include intraarterial thrombolysis with or without the help of ultrasonography, or thrombectomy instruments¹. Intraarterial thrombectomy is conducted using Fogarty balloon catheter, which is reported to be

efficient for the management of acute arterial embolism in lower extremities, especially if it involves single major blood vessel³. However, this technique has limitations due to the possibilities of the presence of thrombus residues, blood vessels trauma due to the passage of balloon catheter, chronic atherosclerosis, which will eventually reduce the success rates of management. Therefore, nowadays, a new technique is introduced. Hybrid procedure is a technique combining endovascular procedures to correct the abnormalities with the help of angiography as well as thrombectomy surgical procedure. Thus, a literature search from appropriate medical research database is necessary to find articles related to the case we are

Figure 1. EBCR schematic design.

reporting, to determine which procedure is the best management, hybrid procedure or thrombectomy.

METHOD

This study is an evidence-based case report (EBCR). The schematic design of this report is shown in Figure 1. This study reported an acute limb ischemia case which was intervened by surgical thrombectomy and over-the-knee amputation. The case management was then analyzed retrospectively using level of evidence priority according to Oxford Centre For Evidence Based Medicine 2011. The case that was used for the report originated from a patient who came to the Emergency Department of Cipto Mangunkusumo National Hospital who had undergone surgical procedure in 2015, see the Case Illustration.

Literature search and selection was conducted using database websites such as Science Direct, Clinical Key, Medline, Springer, Proquest, and Cochrane, using the keywords "acute limb ischemia" AND "thrombectomy" OR "hybrid procedure". From the database websites, we procured a number of articles, which then were screened using our inclusion criteria, which included: literature available in English and published in the last 10 years, research was conducted on humans, and the articles were available as full-text. Articles were sorted to prevent duplications. Resulting articles would be analyzed to discuss the outcome of the management of the reported case using literature sources for comparison. Strategy to find the articles were shown in Figure 2.

Case Illustration

A 57-years female came with the chief complaint progressive blackening of right leg and feet since three days before coming to the hospital, accompanied with pain and numbness. Intermittent claudication was found in the patient. Subject was known to have type 2 diabetes and hypertension since

2011, but they were not controlled. General status of patient was within normal limits. Local status examination on right inferior extremity, there was blackness up to right medial cruris observed. On palpation, the extremity was colder than left inferior extremity, see Figure 3.

Arterial pulsation and *Ankle Brachial Index* (ABI) of the lower extremities can be observed from the Table 1.

Table 1. Arterial pulsation and ABI of patient's lower extremities

	Right	Left
Femoral artery	++	++
Popliteal artery	-	++
Posterior tibial artery	-	+
Dorsal pedis artery	-	+
ABI	-	0,8

ABI = *Ankle Brachial Index*

Laboratory examination results showed hemoglobin 12,9 mg/dL, leukocyte $11.400 \times 10^3/\mu\text{L}$, thrombocyte $272.000 \times 10^3/\mu\text{L}$, fibrinogen 399,2 mg/dL, D-dimer 0,3 mg/L, ureum 46 mg/dL, and creatinine 0,9 mg/dL. Pre-operative CT angiography result showed intraluminal thrombus in right communal femoral artery until superficial femoral artery and 1/3 of profound proximal artery; total occlusion starting from right antero-posterior trifurcation until right peroneal artery; as well as total occlusion in 1/3 proximal to distal of anterior tibial artery and left peroneal artery. Afterwards, amputation was done above the knee level. At the same time, through longitudinal incision on the right inguinal area, superficial femoral and profound artery were identified; while through transverse incision on

Figure 2. Strategy pathway of literature search

common femoral artery, we found a thrombus which had clogged the whole lumen, Figure 4, 5.

Afterwards, Fogarty catheter was inserted into superficial femoral artery and thrombectomy by expanding the Fogarty balloon catheter while pulling it proximally was conducted. A thrombus was obtained, Figure 5.

The procedure was continued by inserting the catheter into profound femoral artery (no thrombus was found); in common femoral artery, there was found thrombus, and post thrombectomy blood flow was smooth. Subject was then admitted into inpatient ward for five days.

Clinical Question

Based on case illustration, the clinical question was formulated as:

"How is the outcome of subject with acute limb ischemia post hybrid procedure compared with thrombectomy?"

RESULTS

Literature search in Science Direct website resulted in 212 articles, with 160 articles fulfilling the inclusion criteria. There were 13 meta-analysis, 23 systematic reviews, 15 randomized-controlled trials (RCTs) and 109 case reports. Literature search in Clinical Key website resulted in 304 articles, with 159 articles fulfilling the inclusion criteria. There were 8 meta-analysis, 26 systematic reviews, 22 RCTs, and 103 case reports. Meanwhile, literature search in Medline website resulted in 641 articles, with 288 articles fulfilling the inclusion criteria. There were 17 meta-analysis, 34 systematic reviews, 26 RCTs, and 211 case reports. On the other hand, literature search in Springer website resulted in 212 articles, with 126 articles fulfilling the inclusion criteria. There were 11

meta-analysis, 16 systematic reviews, 28 RCTs, and 71 case reports. Furthermore, literature search in Proquest website resulted in 29 articles, with all 29 articles fulfilling the inclusion criteria. There were 5 meta-analysis, 13 systematic reviews, 6 RCTs, and 5 case reports. However, literature search in Cochrane website failed to procure any related articles with the keywords as previously mentioned.

The articles collected were then analyzed for their relevance to the case illustration. There were two articles which were found to be most relevant to the case, both from Science Direct and Clinical Key website. It was decided to use the article from Clinical Key website to avoid duplication.

The inclusion criteria for the literature search were as following: 1). the literature was available in English, 2). the research was conducted on humans, and 3). the article must be available in full text so that screening could be done to avoid any duplication. Afterwards, an analysis was conducted to elaborate the outcome of the management of the reported case using literature sources as comparison.

The end results of literature search were two articles which were quite relevant to the clinical question. The first article was written by De Donato in the year 2014, involving 322 subjects. In this article, the intervention conducted was a combination of thrombectomy and endovascular technique (hybrid procedure) and thrombectomy only as comparison. Groups which underwent hybrid procedure consisted of 201 subjects, while the other 112 subjects only underwent thrombectomy. The outcome of this article was early complications (mortality in the first 30 days after procedure and complications during in-patient care, mortality in five years, primary patency, secondary patency, and limb salvage rate).

De Donato research concluded the mortality in the first 30 days in the group which underwent hybrid procedure was significantly ($p = 0.05$) lower

Figure 3. a) Clinical feature of the patient's lower extremities; b) CT angiography of the lower extremities.

(3.3%) than group which underwent only thrombectomy, which was 4.4%. Meanwhile, the complications during in-patient care were also lower in the group receiving hybrid procedure (13.8%) compared to 15.1% in the group which underwent thrombectomy procedure.

There was no significant difference regarding five-years survival rate between the two groups, even though when compared from the percentage, the group which underwent hybrid procedure had higher survival rate (84% vs. 80.9%). The patency of blood flow post procedure after five years in the group which underwent hybrid procedure was also significantly higher (87.1%) compared to the group which underwent thrombectomy, which was only 66.3% (p -value < 0.01 ; 95% CI). Moreover, secondary patency in the group which underwent hybrid procedure was also significantly higher (96.5%) compared to the group which underwent thrombectomy, which was 88.8% (p -value < 0.01 , 95% CI). Limb salvage rate was also higher in the group which underwent hybrid procedure (91.9%) compared to 82.3% in the group which underwent thrombectomy (p -value = 0.03, 95% CI).

The second article was written by Taha, which was published in the year 2015. Total number of subjects in this article was 443 subjects. Subjects which underwent thrombectomy therapy were compared with patients which underwent thrombectomy and endovascular techniques (hybrid procedure). The group which underwent hybrid procedure consisted of 147 subjects, while the other 296 subjects underwent thrombectomy only. The outcomes in this article were success rate of procedure, incidence of complications post surgery, duration of hospital stay, patency of blood flow, number of amputations, 30-days mortality rate, and one-year mortality. The success rate of procedure in the group which underwent open re-vascularization

(thrombectomy) was higher (88.4%) compared to the group which underwent endovascular re-vascularization (hybrid procedure), which was 80.52% with p -value = 0.028. However, the number of amputations within the first 30 days in the group which underwent hybrid procedure were two-fold lower than the group which underwent thrombectomy which was 6.49% vs. 13.5% (p -value < 0.023). Meanwhile, the number of amputations after one year in the group which underwent hybrid procedure were also lower (12.99%) compared to (19.63%) in the group which underwent thrombectomy.

The 30-days and two years mortality rate in the group which underwent hybrid procedure were significantly lower compared to the group which underwent thrombectomy. The 30-days mortality rate in the group which underwent thrombectomy was 13.2% compared to 5.4% in the group which underwent hybrid procedure ($p = 0.012$). The two-years mortality rate of the group which underwent hybrid procedure (18.7%) was significantly lower than the group which underwent thrombectomy (40.5%) (p -score < 0.001). Meanwhile, there was no significant difference in primary closing after two years between the group which underwent hybrid procedure and the group which underwent thrombectomy (38% vs. 48%; p -value < 0.38).

DISCUSSION

Subjects diagnosed with acute limb ischemia can still be commonly found in Indonesia coming in delayed condition, as in the reported case. The mortality rate of these cases was still quite high, reaching up to 15%, with amputation rate varying around 25-30%.⁴⁻⁵ This phenomenon contrasted with other countries, where patient came to the hospital in early phase of the condition, which resulted in better prognosis.

Figure 4. Thrombus was clogging the whole lumen of common femoral artery

Diagnosis establishments, surgical techniques, and pre-operative preparation has developed greatly in the last few years. In clinical practice, there are discrepancy between the success of thrombectomy surgery and clinical outcome. This therapeutic procedure is relatively easy to conduct and has high technical success rate. The disadvantage of this procedure is that patients who underwent the procedure may still have quite high mortality and amputation rate.

Other therapeutic option which recently commonly used is a combination between surgery and endovascular technique, which is also called hybrid procedure. In a few reports, this therapy may decrease the incidence of amputation and mortality. The disadvantage of this procedure is that this procedure can not be conducted on patients with hypersensitivity to contrast agents and renal disorders.⁶⁻⁸

The two selected articles were analyzed based on their validity, importance, and applicability. The first article by De Donato was valid because it was designed as prospective cohort and its research subjects were selected using consecutive sampling method.² Meanwhile, the research by Taha was designed as a retrospective cohort and its research subjects were selected using randomized consecutive sampling method.⁹ For topics such as this, these methods were quite appropriate since randomization would be very hard to apply. Moreover, these methods were also able to evaluate multiple outcomes, as well as analyze the relationship between variables within a certain time limit. The two articles divided the subjects into two groups: the group which underwent hybrid procedure and the group which underwent thrombectomy only. Operational definitions and measured outcomes had been explained in the Methods section.

Combination therapy for patients diagnosed with acute limb ischemia was first introduced by Parsons in the year 1996 using intraoperative fluoroscopy and fluoroscopically-assisted thrombectomy.²⁻³ This hybrid procedure could increase the success rate of thrombectomy only. This technique was also able to minimize injuries to blood vessel when clot removal was conducted.

According to a few literature sources, post thrombectomy angiography not only is able to identify residual distal thrombus, but also able to identify incomplete recanalization in more proximal arteries,

Figure 5. Thrombus which had been extracted by thrombectomy, number was shown in centimeter (cm).

as well as evaluating steno-occlusive lesions after clot removal. In a small number of cases, angiography may even identify blood vessel injuries due to balloon catheter passage.¹⁻⁵ After this technique was introduced, angiography becomes a routine procedure after thrombectomy, even though its clinical outcome is still unclear.

These two articles proved that there were significant outcome differences between patients who underwent hybrid procedure (thrombectomy and endovascular procedure) compared to patients who underwent thrombectomy only. Thirty-days and two-years mortality rate in patients who underwent hybrid procedure were significantly lower compared to patients who underwent thrombectomy only. However, according to De Donato, the decrease of five-years mortality rate in patients who underwent hybrid procedure was not statistically significant.^{2,9} This discrepancy may become the basis for future researches since there are still very few researches regarding hybrid procedure in patients diagnosed with acute limb ischemia, which included follow-up up to five years after the procedure. However, in general, from these two articles, we can conclude that hybrid procedure is able to decrease patients' mortality rate.

Furthermore, these two articles also proved that complication and amputation rate were also lower in the group which underwent hybrid procedure compared to thrombectomy only. Moreover, according to Taha, the number of amputations in the first 30 days could be further cut down up to two-fold by using hybrid procedure.⁹ Although, also according to Taha, the number of amputations after one year was not significant. Patency of blood flow in the group which underwent hybrid procedure was also more superior compared to the group which underwent thrombectomy only. One of the reasons for this good clinical outcome was because the percutaneous pharmacological or mechanical thrombolysis, which was conducted after surgery, might increase the number of thrombus flushed through distal blood vessels.

Discussion regarding the two articles showed strong level of evidence, and studying cases which were similar to the case illustration reported, with similar characteristics, using hybrid procedure, can be used as references for the case. The articles also showed that hybrid procedure is suitable to be applied in the reported case, as well as showing lower morbidity and mortality rate when compared to thrombectomy. Patients with acute limb ischemia whose condition are similar to the one shown in the

reported case might benefit from hybrid procedure, so that morbidity and mortality rate can be decreased.

These researches hopefully can be the basis for hybrid procedure establishments in Indonesia. Hybrid procedure has been proven to show many advantages compared to thrombectomy only for subjects whose condition are similar to the subject in the reported case. This article can be used a reference for the procurement of the necessary tools and facilities as well as clinical protocols for the management of patients diagnosed with acute limb ischemia.

CONCLUSION

In conclusion, for patients with acute limb ischemia, a combination of thrombectomy and endovascular procedure has better clinical outcome compared to thrombectomy only. Hybrid procedure therapy can decrease mortality, complications, number of amputations, as well as increase blood flow patency. However, a few outcomes, such as five-years mortality rate has no significant differences

between the two groups. Cases of acute limb ischemia which are similar to the reported cases might benefit from hybrid procedure, in order to deliver the best therapy for the patients.

CONFLICT OF INTEREST

The author states the original work, and there is no conflict of interest in doing this research.

ORCID ID OF AUTHORS

Purnama Satria Bakti
<https://orcid.org/0000-0002-9372-3720>

Nyityasmono Tri Nugroho
<https://orcid.org/0000-0001-8876-9698>

Dedy Pratama
<https://orcid.org/0000-0003-2043-3084>

REFERENCES

1. Baunmann F, Sharpe E, Pena C, Samuels S, James F. Technical Results of Vacuum-Assisted Trombektomi for Arterial Clot Removal in Patients with Acute limb ischemia. *J Vasc Interv Radiol.* 2016;20:1-6.
2. Donato G, Setacci F, Sirignano P, Galzerano G, Massaroni R, Setacci C. The Combination of Surgical Embolectomy and Endovascular Techniques May Improve Outcomes of Patients with Acute Lower Limb Ischemia. *J Vasc Surg.* 2014;59:729-36.
3. Daly B, Patel M, Prasad A. The Use of the Trellis-6 Trombektomi Device in the Management of Acute limb ischemia due to Native Vessel Occlusion: Challenges, Tips, and Limitations. *Cardiovasc Interv Ther.* 2012;1-6.
4. Gupta R, Hennebry TA. Percutaneous Isolated Pharmaco-Mechanical Thrombolysis-Trombektomi System for the Management of Acute Arterial Limb Ischemia: 30-Day Results From a Single-Center Experience. *Cardiovasc Interv Ther.* 2012;1-8.
5. Kwak JW, Chung HW, Lee SH, Kim YH, Cho SB, Seo TS, Jo W, dkk. A new endovascular strategy utilizing a hybrid procedure for long segmental occlusion by acute arterial thromboembolism in the lower extremity. *Jpn J Radiol.* 2016;34:494-502.
6. Leung DA, Blitz RL, Nelson T, Amin A, Soukas PA, Nanjundappa A, dkk. Rheolytic Pharmacomechanical Trombektomi for the Management of Acute limb ischemia: Results from the PEARL Registry. *Jevt.* 2015; 1-12.
7. Lichtenberg M, Stahlhoff W, Boese D, Hailer B. Twelve months outcome after percutaneous mechanical trombektomi for treatment of acute femoropopliteal bypass occlusion. *Cardiovasc Interv Ther.* 2013;28:178-83.
8. Shin HS, Kyoung KH, Suh BJ, Jun SY, Park JK. Acute limb ischemia: Surgical Thromboembolctomy and the Clinical Course of Arterial Revascularization at Ankle. *Int J Angiol.* 2013;22:109-14.
9. Taha AG, Byrne RM, Efthymios D, Avgerinos ED, Marone LK, Makaroun MS, dkk. Comparative effectiveness of endovascular versus surgical revascularization for acute lower extremity ischemia. *J Vasc Surg.* 2015;61:147-54.
10. Slegt JD, Flu HC, Veen EJ, Ho GH, Hans GW, Groot D, dkk. Adverse events/ after treatment of patients with acute limb ischemia. *Annals of Vasc Surg.* 2014:1-26.